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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,491	WU ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,10-14,16-20,23-25 and 27* is/are pending in the application.

4a) Of the above claim(s) *14,16-20,23 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,10-13,24 and 25* is/are rejected.

7)☐ Claim(s) *12 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0406*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Invention I, in their response of February 29, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). It is acknowledged that Applicants have amended Claims 1, 2, and 7. Claims 1-5, 7, 10-14, 16-20, 23-25, and 27 are pending. The elected invention is directed to the protease polypeptide of SEQ ID NO: 2 and variants thereof. Claims 14, 16-20, 23, and 27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-5, 7, 10-13, 24, and 25 are hereby examined.

Priority

The priority date granted for the instant invention is October 22, 2004, the filing date of PCT/DK04/00730, which disclosed the elected invention.

Drawing-Objections

All drawings are objected to because the abbreviations therein are not defined by the drawings or the figure legends and the figure legends are not sufficiently descriptive of the drawings. The figure legends should be sufficiently descriptive of the drawings such that public need not search through the disclosure for an explanation.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object e.g., "We claim" or "The claims are".

Claim 12 is objected to for poor grammar. The phrase "–when tested in 'Example V stability in detergent'–" would be more clearly stated as ", when tested using the method disclosed in Example V,".

Claim 25 is object to for "an amylase or a mixture", which would be better stated as "an amylase, or a mixture".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5, 7, and 10-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The proteases recited in said claims are likely to occur in nature and, thus, the recited invention fails to show the "hand of man".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7, 10-13, 24, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 1 and 10, the phrases "low stringency" and "medium stringency" and "high stringency" renders the claim indefinite as these terms are unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization conditions, will not necessarily hybridize under different conditions.

The hybridization conditions disclosed in paragraphs [006-0069] do not describe the conditions to be used for low, medium, or high stringency hybridization using a short probe; the conditions recited in Claims 1 and 10 are not defined. Thus, Claims 1 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claims 2-5, 7, 10-13, 24, and 25, as dependent from Claim 1, are indefinite for the same reason.

For Claims 1 and 10, the phrase "a complementary strand of …SEQ ID NO: 1" renders the claim indefinite. It is unclear whether said phrase means "any a complementary strand, having any length, of …SEQ ID NO: 1" or "the full-length complementary strand of …SEQ ID NO: 1". The skilled artisan would not know the metes and bounds of the recited invention. Claims 2-5, 7, 11-13, 24, and 25, as dependent from Claim 1, are indefinite for the same reason. For purposes of examination, it is assumed that the phrase means "the full-length complementary strand of …SEQ ID NO: 1".

For Claim 5, it is unclear whether the phrase "comprising a substitution ...of one or more amino acid residues" modifies the parent protease or the variant protease. The skilled artisan would not know the metes and bounds of the recited invention. Claim 12, as dependent from Claim 5, is indefinite for the same reason. For purposes of examination, it is assumed that "comprising a substitution ...of one or more amino acid residues" modifies the variant protease.

For Claim 11, the phrase "trypsin like" renders the claim indefinite. The description of said phrase by the specification is only exemplary [0162]. The skilled artisan would not know the metes and bounds of the recited invention.

For Claims 12 and 13, the phrase "after storage at 35°C" renders the claim indefinite because neither the claims nor the specification disclose the duration of time for the storage at 35°C. The skilled artisan would not know the metes and bounds of the recited invention.

Claims 12 and 13 are indefinite because the specific steps and reagents to be used in determining the "residual activity" are not disclosed. Neither the claims nor the specification disclose the concentration of enzyme to be used, what substrate or conditions are to be used, what the "reference sample" [0307] is, or what activity parameter, e.g., K_m, V_{max}, K_{cat}, or other parameter, is to be compared. The skilled artisan would not know the metes and bounds of the recited invention.

Claims 2-5, 7, 10, 11-13, and 25 are rendered indefinite by improper antecedent usage as follows.

For Claims 2-5, 7, 10, and 11, the phrase "A protease according to claim 1" should be corrected to "The protease according to claim 1".

For Claim 12, the phrase "A protease according to any of the preceding claims" should be corrected to "The protease according to any of the preceding claims".

For Claim 13, the phrase "A protease according to claim 11" should be corrected to "The protease according to claim 11".

For Claim 25, the phrase "A composition according to claim 24" should be corrected to "The composition according to claim 24".

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1, 2, 5, 7, 11-13, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any variant thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1, 2, 7, 11-13, 24, and 25 are so broad as to encompass any protease comprising a sequence having (i) at least 85% homology to SEQ ID NO: 2, (ii) encoded by a polynucleotide that hybridizes under low stringency conditions to SEQ ID NO: 1, or (iii) having up to 50 amino acid substitutions of SEQ ID NO: 2 (77% homology). Claim 5 is so broad as to encompass any protease comprising a variant of SEQ ID NO: 2 having any number of substitutions, deletions, or

insertions. Claim 10 is so broad as to encompass any protease comprising any polypeptide encoded by any polynucleotide that hybridizes under medium stringency conditions to SEQ ID NO: 1. It is noted that by use of "comprising" language, these claims encompass proteases wherein the activity is not derived from the sequence homologous to SEQ ID NO: 2.

The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 2 and the nucleotide sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 1, 2, 7, 11-13, 24, and 25, which encompasses all proteases comprising a sequence having at least 85% homology to SEQ ID NO: 2, encoded by a polynucleotide that hybridizes under low stringency conditions to SEQ ID NO: 1, or has up to 50 amino acid substitutions of SEQ ID NO: 2. The specification does not support the broad scope of Claim 5, which encompasses all proteases comprising a variant of SEQ ID NO: 2 having any number of substitutions, deletions, or insertions. The specification does not support the broad scope of Claim 10, which encompasses all proteases comprising any polypeptide encoded by any polynucleotide that hybridizes under medium stringency conditions to SEQ ID NO: 1. The specification does not support the broad scope of Claims 1, 2, 5, 7, 10-13, 24, and 25 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting the desired activity; (B) the general tolerance of the desired activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptide with an enormous number of amino acid modifications of the polypeptide of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in

the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 7 is further rejected under 35 U.S.C. 112 first paragraph/enablement, for the following reasons. The invention appears to employ novel vectors comprised within novel host cells. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

Written Description

Claims 1, 2, 7, 11-13, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of proteases comprising a sequence having at least 85% homology to SEQ ID NO: 2, encoded by a polynucleotide that hybridizes under low stringency conditions to SEQ ID NO: 1, having up to 50 amino acid substitutions of SEQ ID NO: 2, a variant of SEQ ID NO: 2 having any number of substitutions, deletions, or insertions, or any polypeptide encoded by any polynucleotide that hybridizes under medium stringency conditions to SEQ ID NO: 1. The specification teaches the

structure of only a single representative species of such proteases. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a protease comprising a variant of SEQ ID NO: 2. Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1, 2, 7, 11-13, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of proteases comprising a sequence having at least 85% homology to SEQ ID NO: 2, encoded by a polynucleotide that hybridizes under low stringency conditions to SEQ ID NO: 1, having up to 50 amino acid substitutions of SEQ ID NO: 2, a variant of SEQ ID NO: 2 having any number of substitutions, deletions, or insertions, or any polypeptide encoded by any polynucleotide that hybridizes under medium stringency conditions to SEQ ID NO: 1. The specification does not contain any disclosure of the function of all protein sequences that have at least 85% homology to SEQ ID NO: 2, are encoded by a polynucleotide that hybridizes under low stringency conditions to SEQ ID NO: 1, have up to 50 amino acid substitutions of SEQ ID NO: 2, is variant of SEQ ID NO: 2 having any number of substitutions, deletions, or insertions, or any polypeptide encoded by any polynucleotide that hybridizes under medium stringency conditions to SEQ ID NO: 1. Therefore, many functionally unrelated polypeptide are encompassed within the scope of

these claims, including partial peptide sequences. The specification discloses the function of only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7, 10-13, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Isono et al, 1972 as evidenced by Isono et al, 1972 and Esaki et al, 1994. Isono et al teach an alkaline protease isolated from Fusarium solani that shows activity in a detergent composition (Table 5). More likely than not, Isono's F. solani alkaline protease has thermostability, since an alkaline protease isolated from Fusarium sp has thermostability (Isono et al; Figs 3 & 4) and an aminotransferase isolated from F. solani has thermostability (Esaki et al; Abstract). Since the protease of SEQ ID NO: 2 is from F. solani, the skilled artisan would believe that, more likely than not, Isono's protease isolated from F. solani is the same as the protease of SEQ ID NO: 2

herein. Therefore, Claims 1-5, 7, 10-13, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Isono et al, 1972 as evidenced by Isono et al, 1972 and Esaki et al, 1994.

Claims 1, 5, and 10-13 are rejected under 35 U.S.C. 102(b), as being anticipated by Hastrup et al, 1997 as evidenced by Christakopoulos et al, 1996. Hastrup et al teach a F. oxysporum alkaline protease (Claim 4) having 75.2% homology to SEQ ID NO: 2 herein, which is encoded by a polynucleotide having 56.8% homology to SEQ ID NO: 1 herein (see enclosed alignments). Since enzymes isolated from F. oxysporum are known to be thermostable (Christakopoulos et al; Abstract), the skilled artisan would believe that, more likely than not, the F. oxysporum alkaline protease of Hastrup et al is also thermostable. Therefore, Claims 1, 5, 7, 10-13 are rejected under 35 U.S.C. 102(b), as being anticipated by Hastrup et al, 1997 as evidenced by Christakopoulos et al, 1996.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isono et al, 1972 or Hastrup et al, 1997 in view of Okuda et al, 2004 (FD 12-MAR-2003). The teachings of Isono et al and Hastrup et al are described above. Neither Isono et al nor Hastrup et al teach a detergent composition comprising their alkaline protease and, optionally, further comprising a cellulase, lipase, cutinase, oxidoreductase, another protease, an amylase, or a mixture thereof. Okuda et al teach a detergent composition comprising an alkaline protease and, optionally,

further comprising a protease other than the alkaline protease of their invention, an hydrolase, reductase, oxidase, cellulase, cutinase, amylase, lipase, or a mixture thereof [0065]. It would have been obvious to a person of ordinary skill in the art to combine the teachings of Isono et al or Hastrup et al with the teachings of Okuda et al to produce a detergent composition comprising an alkaline protease of Isono et al or Hastrup et al and, optionally, further comprising a cellulase, lipase, cutinase, oxidoreductase, another protease, an amylase, or a mixture thereof. Motivation to do so derives from the simple substitution of the alkaline protease of Okuda et al with the alkaline protease of Isono et al or Hastrup et al (*KSR International v. Teleflex Inc*). The expectation of success is high, as detergent compositions comprising an alkaline protease and, optionally, further comprising a cellulase, lipase, cutinase, oxidoreductase, another protease, an amylase, or a mixture thereof were known in the art and used for cleaning methods. Therefore, Claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isono et al, 1972 or Hastrup et al, 1997 in view of Okuda et al, 2004 (FD 12-MAR-2003).

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652